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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/507,442

03/15/2006

Edward A. Hunter

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DLA PIPER LLP (US)

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EXAMINER

SKOWRONEK, KARLHEINZ R

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/507,442	Applicant(s) HUNTER ET AL.	
	Examiner KARLHEINZ R. SKOWRONEK	Art Unit 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 16 July 2010.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3 and 5 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3 and 5 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claim Status

Claims 1-10 are pending.

Claims 1-10 have been examined.

Claims 1-10 are rejected.

Priority

This application accepted on 15 March 2006 as the 35 USC 371 filing of PCT/US03/07968, filed on 13 March 2003, and claims the benefit of US Provisional Application No. 60/363,889, filed on 13 March 2002.

Objections to the Specification

The use of the trademarks PENTIUM (p. 8, 19), WINDOWS (p. 9), NIKON (p.10, 19, 20), VISUAL C++ (p. 51), and MICROSOFT (p. 51) have been noted in this application. They should be capitalized wherever they appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 101

Response to Arguments

The rejection of claim 1-5 is withdrawn upon reconsideration of the claims in view of the recent Supreme court decision, In Re Biliski. Taken as a whole, the claims are directed to a method performed by an automated microscopy platform.

Claim Rejections - 35 USC § 112

Response to Arguments

The rejection of claims 4 and 9 as indefinite under 35 UC 112, second paragraph is withdrawn in view of the cancellation of claims 4 and 9.

The Rejection of claims 6-10 as indefinite and lacking written description under 35 USC 112, first and second paragraphs is withdrawn in view of the cancellation of claims 6-10.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-3 and 6-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Giuliano et al. (US PAT 6,416,959), in view of Lee et al. (US PAT 5,528,703), and in view of Sudbo et al. (Analytical Cellular Pathology, 21, p. 71–86, 2000).

The claims are directed to a method and system for measuring cell activity in which the cells in an image are segmented; separating segmented overlapping cells, and measuring the translocation of cellular material between a first and second region of the cell caused by an agent. In an embodiment, segmenting includes enhancing the contrast between the first and second compartments and the background. In an embodiment, separating includes tessellation.

Giuliano et al. shows a method and system for measuring cell activity by image analysis. Giuliano et al. shows the cells in an image are segmented (col. 21, line 50-52). Giuliano et al. shows the translocation of cellular material between a first and second region of the cell caused by an agent is measured (col. 25, 52-67). Giuliano et al shows the cellular material in a first region of interest is compared to the cellular material in a second region of interest (col. 18 line 13-46)

Giuliano et al. does not show separating segmented overlapping cells.

Lee et al. shows a method of identifying objects in images. Lee et al. shows cells that are overlapping in an image are separated (col. 5, line 38-52). Lee et al shows this has the benefit of reducing the impact of overlapping cells on parameter determination (col. 5, line 46-47).

Giuliano et al. in view of Lee et al. does not show separating by tessellation.

Sudbo et al. is directed to a method of separating cells in an image using the tessellation techniques of Voronoi Diagram (VD) construction and Delaunay triangulation (figures 1 and 2; p. 73, col. 1-p. 74, col. 1). Sudbo et al. shows segmenting includes enhancing the contrast between any element to be detected and the background (p. 72, col. 2). Sudbo et al. shows the Voronoi Diagram is the most informative tool for exploring tissue structure.

It would have been obvious to one of ordinary skill in the art at the time of invention to modify the method and system for measuring cell activity of Giuliano et al. with the separation of overlapping cells of Lee et al. because Lee et al. shows doing so has the benefit of reducing the impact of overlapping cells on parameter determination. It would have been further obvious to one of ordinary skill in the art at the time of invention to modify the method and system for measuring cell activity of Giuliano et al. and separation of overlapping cells of Lee et al. using the tessellation technique of Voronoi Diagrams of Sudbo et al. because Sudbo et al. shows the Voronoi Diagram is the most informative tool for exploring tissue structure. It would have been further obvious to one of ordinary skill in the art at the time of invention to modify the method and system for measuring cell activity of Giuliano et al. and separation of overlapping

Art Unit: 1631

cells of Lee et al. using the tessellation technique of Voronoi Diagrams of Sudbo et al. because all the claimed elements were known, in the prior art, and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded nothing more than predictable results to one of ordinary skill in the art at the time of the invention.

Claims 4-5 and 9-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Giuliano et al., in view of Lee et al., and in view of Sudbo et al. As applied to claims 1-3 and 6-8 above, and further in view of Pohl et al. (Pharmaceutical research, Vol. 16, No. 2, p. 327-332, 1999).

An embodiment of the claims is directed to measuring the fractional intensity of cellular materials and comparing the fractional intensities. In another embodiment, the claims are directed to segmenting that includes enhancing background and separating that includes tessellating.

Giuliano et al., in view of Lee et al., and in view of Sudbo et al. as applied to claims 1-3 and 6-8 above show a method of image analysis for measuring cell activity in response to an agent in which segmenting includes enhance contrast with the background and separating that includes tessellation.

Giuliano et al., in view of Lee et al., and in view of Sudbo et al. does not show the measurement of a fractionalized intensity.

Pohl et al. shows a measurement of fractional intensity. Pohl et al. shows the fractional intensity is the measure of fluorescence intensity of a region of interest divided

Art Unit: 1631

the measure of total fluorescence intensity (p.330, col. 1). Pohl shows in figure 3 the successful use of fractional intensity to compare different regions of interest.

It would have obvious to one of ordinary skill in the art at the time of invention to modify the method of image analysis for measuring cell activity in response to an agent of Giuliano et al., in view of Lee et al., and in view of Sudbo et al. as applied to claims 1-3 and 6-8 above with the fractional fluorescence intensity measurements of Pohl et al. because all the claimed elements were known, in the prior art, and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded nothing more than predictable results to one of ordinary skill in the art at the time of the invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

Art Unit: 1631

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-3 and 5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Giuliano et al., in view of Lee et al., in view of Sudbo et al., and in view of Pohl et al.

The claims are directed to a method and system for measuring cell activity in which the cells in an image are segmented; separating segmented overlapping cells, and measuring the translocation of cellular material between a first and second region of the cell caused by an agent. In an embodiment, segmenting includes enhancing the contrast between the first and second compartments and the background. In an embodiment, separating includes tessellation.

Giuliano et al. shows a method and system for measuring cell activity by image analysis. Giuliano et al. shows the cells in an image are segmented (col. 21, line 50-52). Giuliano et al. shows the translocation of cellular material between a first and second region of the cell caused by an agent is measured (col. 25, 52-67). Giuliano et al shows

Art Unit: 1631

the cellular material in a first region of interest is compared to the cellular material in a second region of interest (col. 18 line 13-46).

Giuliano et al. does not show separating segmented overlapping cells.

Lee et al. shows a method of identifying objects in images. Lee et al. shows cells that are overlapping in an image are separated (col. 5, line 38-52). Lee et al shows this has the benefit of reducing the impact of overlapping cells on parameter determination (col. 5, line 46-47).

Giuliano et al. in view of Lee et al. does not show separating by tessellation.

Sudbo et al. is directed to a method of separating cells in an image using the tessellation techniques of Voronoi Diagram (VD) construction and Delaunay triangulation (figures 1 and 2; p. 73, col. 1-p. 74, col. 1). Sudbo et al. shows segmenting includes enhancing the contrast between any element to be detected and the background (p. 72, col. 2). Sudbo et al. shows the Voronoi Diagram is the most informative tool for exploring tissue structure.

Giuliano et al., in view of Lee et al., and in view of Sudbo et al. does not show the measurement of a fractionalized intensity.

Pohl et al. shows a measurement of fractional intensity. Pohl et al. shows the fractional intensity is the measure of fluorescence intensity of a region of interest divided the measure of total fluorescence intensity (p.330, col. 1). Pohl shows in figure 3 the successful use of fractional intensity to compare different regions of interest.

It would have been obvious to one of ordinary skill in the art at the time of invention to modify the method and system for measuring cell activity of Giuliano et al.

Art Unit: 1631

with the separation of overlapping cells of Lee et al. because Lee et al. shows doing so has the benefit of reducing the impact of overlapping cells on parameter determination. It would have been further obvious to one of ordinary skill in the art at the time of invention to modify the method and system for measuring cell activity of Giuliano et al. and separation of overlapping cells of Lee et al. using the tessellation technique of Voronoi Diagrams of Sudbo et al. because Sudbo et al. shows the Voronoi Diagram is the most informative tool for exploring tissue structure. It would have obvious to one of ordinary skill in the art at the time of invention to modify the method of image analysis for measuring cell activity in response to an agent of Giuliano et al., in view of Lee et al., and in view of Sudbo et al. with the fractional fluorescence intensity measurements of Pohl et al. because all the claimed elements were known, in the prior art, and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded nothing more than predictable results to one of ordinary skill in the art at the time of the invention.

Response to Arguments

Applicant's arguments filed 16 July 2010 have been fully considered but they are not persuasive. Applicant argues Giuliano et al. in view of Lee et al. in view of Sudbo et al. and in view of Pohl et al. fail to show the elements of the claim. The argument is not persuasive. Giuliano et al. shows an automated microscopy platform that measures cell activity. Specifically Giuliano et al shows measurements of the translocation of cellular material from the cytoplasm into the nucleus. Giuliano et al shows the measurement of

Art Unit: 1631

a first intensity for a cellular material in a first compartment and a second intensity of the cellular material in a second compartment (col. 18, line 13-46). Giuliano et al. show images generated by the microscopy platform are segmented (col. 17, line 30-47). Giuliano et al. shows the comparison of distinct cellular compartments by fractional comparison (col. 18, line 13-46). Giuliano et al. shows a fractional intensity as a ration of the intensity of a first compartment of a cell to the difference of the intensity of the first compartment and the intensity of the second compartment. The compartments measured by Giuliano et al. are regions of interest. Similarly, Pohl et al. shows the measurement of intensities in two distinct regions of interest. Pohl et al shows that fractional intensity is calculated by determining the ratio of the intensity of first region of interest to the sum of the first region of interest and the second region of interest. The showing in both Giuliano et al. and Pohl et al. of the determination of ratios of a region of interest to either the sum or difference demonstrate the calculation of fractional localized intensities was known in the art and known to be applied in the microscopic imaging of biological material. Applicant argues the calculations are inaccurate and error prone as described in the specification. The argument is not persuasive. While the claims are read in light of the specification, limitations from the specification are not read into the claims. Applicant similarly argues that Fractional Localized Intensity of Cellular compartments (FLIC) is distinguished from Giuliano et al. in view of Lee et al. in view of Sudbo et al. and in view of Pohl et al. by the application of image segmentation and the calculation of fractional intensity as exemplified in the specification as equation 1. The argument is not persuasive. The claims broadly recite the determination an intensity for

Art Unit: 1631

two compartments. The intensity determination as intantly claimed are not distinguished from the intensity determinations of Giuliano et al. in view of Lee et al. in view of Sudbo et al. and in view of Pohl et al. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Art Unit: 1631

Any inquiry concerning this communication or earlier communications from the examiner should be directed to KARLHEINZ R. SKOWRONEK whose telephone number is (571)272-9047. The examiner can normally be reached on 8:00am-5:00pm Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran can be reached on (571) 272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/KARLHEINZ R SKOWRONEK/
Primary Examiner, Art Unit 1631

31 August 2010

Application/Control Number: 10/507,442
Art Unit: 1631

Page 14